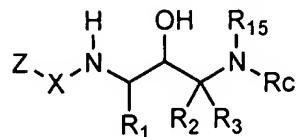


Claim 1. (previously presented) A compound of the formula:



or a pharmaceutically acceptable salt or ester thereof,  
wherein Z is aryl, heteroaryl or heterocyclyl, wherein said groups are optionally substituted with 1 or 2 R<sub>B</sub> groups, wherein, where R<sub>B</sub> at each occurrence is independently selected from halogen, -OH, -OCF<sub>3</sub>, -O-phenyl, -CN, -NR<sub>100</sub>R<sub>101</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, (CH<sub>2</sub>)<sub>0-3</sub>(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, halogen, -OH, -CN, or -NR<sub>100</sub>R<sub>101</sub>;  
where R<sub>100</sub> and R<sub>101</sub> are at each occurrence are independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, or phenyl;  
X is -(C=O)- or -(SO<sub>2</sub>)-;  
wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, -CN, -CF<sub>3</sub>, -OCF<sub>3</sub>, -C<sub>3-7</sub> cycloalkyl, -C<sub>1</sub>-C<sub>4</sub> alkoxy, amino, mono-dialkylamino, aryl, heteroaryl, heterocycloalkyl, wherein each aryl group is optionally substituted with 1, 2 or 3 R<sub>50</sub> groups;

wherein  $R_{50}$  is selected from halogen, OH, SH, CN, -CO- (C<sub>1</sub>-C<sub>4</sub> alkyl), -NR<sub>7</sub>R<sub>8</sub>, -S(O)<sub>0-2</sub>- (C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy and C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy and cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, OH, -NR<sub>5</sub>R<sub>6</sub>, CN, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, NR<sub>7</sub>R<sub>8</sub>, and C<sub>1</sub>-C<sub>4</sub> alkoxy;

wherein R<sub>5</sub> and R<sub>6</sub> are independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; or

wherein R<sub>5</sub> and R<sub>6</sub> and the nitrogen to which they are attached form a 5 or 6 membered heterocycloalkyl ring; and

wherein R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of H; -C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -OH, -NH<sub>2</sub>, and halogen; -C<sub>3</sub>-C<sub>6</sub> cycloalkyl; -(C<sub>1</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl); -C<sub>2</sub>-C<sub>4</sub> alkenyl; and -C<sub>2</sub>-C<sub>4</sub> alkynyl;

wherein each heteroaryl is optionally substituted with 1 or 2 R<sub>50</sub> groups;

wherein each heterocycloalkyl group is optionally substituted with 1 or 2 groups that are independently R<sub>50</sub> or =O;

$R_2$  and  $R_3$  are independently selected from

-H;

-F;

- $C_1-C_6$  alkyl optionally substituted with a substituent selected from the group consisting of -F, -OH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>5</sub>R<sub>6</sub>;

- (CH<sub>2</sub>)<sub>0-2</sub>-R<sub>17</sub>;

- (CH<sub>2</sub>)<sub>0-2</sub>-R<sub>18</sub>;

- $C_2-C_6$  alkenyl or  $C_2-C_6$  alkynyl, wherein each is optionally substituted with an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF<sub>3</sub> and C<sub>1</sub>-C<sub>3</sub> alkoxy;

- (CH<sub>2</sub>)<sub>0-2</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy and -NR<sub>5</sub>R<sub>6</sub>; or

$R_2$ ,  $R_3$  and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from -O-, -S-, -SO<sub>2</sub>-, or -NR<sub>7</sub>-;

where  $R_{17}$  at each occurrence is an aryl group selected from phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl and tetralinyl, wherein said aryl groups are optionally substituted with one or two groups that are independently

-C<sub>1</sub>-C<sub>3</sub> alkyl; -C<sub>1</sub>-C<sub>4</sub> alkoxy; CF<sub>3</sub>; or

-C<sub>2</sub>-C<sub>6</sub> alkenyl or -C<sub>2</sub>-C<sub>6</sub> alkynyl each of which is optionally substituted with one substituent selected from the group consisting of F, OH, C<sub>1</sub>-C<sub>3</sub> alkoxy; or -halogen; -OH; -C≡N; -C<sub>3</sub>-C<sub>7</sub> cycloalkyl; -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl); -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl);

where R<sub>18</sub> is a heteroaryl group selected from pyridinyl, pyrimidinyl, quinolinyl, indolyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl, quinoxaliny, phthalazinyl, imidazolyl, isoxazolyl, oxazolyl, thiazolyl, furanyl, thieryl, pyrrolyl, oxadiazolyl or thiadiazolyl, wherein each of said heteroaryl groups is optionally substituted with one or two groups that are independently

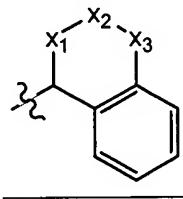
-C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of OH, C≡N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>5</sub>R<sub>6</sub>;

R<sub>15</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub> alkyl, halo C<sub>1</sub>-C<sub>6</sub> alkyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, NH<sub>2</sub>, and -R<sub>26</sub>-R<sub>27</sub>;

wherein  $R_{26}$  is selected from the group consisting of a bond,  $-C(O)-$ ,  $-SO_2-$ ,  $-CO_2-$ ,  $-C(O)NR_5-$ , and  $-NR_5C(O)-$ ,

wherein  $R_{27}$  is selected from the group consisting of  $C_1-C_6$  alkyl,  $C_1-C_6$  alkoxy, aryl  $C_1-C_6$  alkyl, heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently  $C_1-C_4$  alkyl,  $C_1-C_4$  alkoxy, halogen, haloalkyl, hydroxyalkyl,  $-NR_5R_6$ ,  $-C(O)NR_5R_6$ ;

$R_C$  is a group of the formula



wherein  $x_1$ ,  $x_2$ , and  $x_3$  are independently  $-CHR_{245}$ ,  $SO_2$ , or  $NH$ , and wherein the phenyl ring is optionally substituted with 1 or 2  $R_{245}$  groups,

wherein each  $R_{245}$  group is independently selected from the group consisting of

$-H$ ,

$-(CH_2)_{0-4}CO_2C_1-C_4$  alkyl

$-(CH_2)_{0-4}C(=O)C_1-C_4$  alkyl

$-C_1-C_4$  alkyl,

$-C_1-C_4$  hydroxyalkyl,

$-C_1-C_4$  alkoxy,

$-C_1-C_4$  haloalkoxy,

$-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

-C<sub>2</sub>-C<sub>6</sub> alkenyl,  
-C<sub>2</sub>-C<sub>6</sub> alkynyl,  
- (CH<sub>2</sub>)<sub>0-4</sub> aryl,  
- (CH<sub>2</sub>)<sub>0-4</sub> heteroaryl, and  
- (CH<sub>2</sub>)<sub>0-4</sub> heterocycloalkyl

wherein the aryl, heteroaryl or heterocycloalkyl group included within R<sub>245</sub> is optionally substituted with 1, 2, or 3 groups that are independently halogen, C<sub>1-6</sub> alkyl, CN or OH.

Claim 2. (Currently amended) A compound according to claim 1, wherein:

Z is aryl or heteroaryl, wherein each ring is independently optionally substituted with 1 or 2 groups independently selected from halogen, -OH, -OCF<sub>3</sub>, -O-phenyl, -CN, -NR<sub>100</sub>R<sub>101</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, (CH<sub>2</sub>)<sub>0-3</sub>(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, halogen, -OH, -CN, or -NR<sub>100</sub>R<sub>101</sub>.

Claim 3. (original) A compound according to claim 1, wherein X is -(C=O)-.

Claim 4. (original) A compound according to claim 1, wherein:  
R<sub>1</sub> is -C<sub>1</sub>-C<sub>6</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>6</sub> alkyl-heteroaryl, or -C<sub>1</sub>-C<sub>6</sub> alkyl-heterocyclyl, wherein each aryl group at each occurrence is optionally substituted with 1, 2 or 3 R<sub>50</sub> groups;  
wherein R<sub>50</sub> is independently selected from halogen, OH, SH, CN, -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -NR<sub>7</sub>R<sub>8</sub>, -S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, or C<sub>3</sub>-C<sub>8</sub> cycloalkyl;  
wherein the alkyl, alkenyl, alkynyl, alkoxy, or cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, OH, -NR<sub>5</sub>R<sub>6</sub>, CN, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, NR<sub>7</sub>R<sub>8</sub>, and C<sub>1</sub>-C<sub>4</sub> alkoxy;  
wherein R<sub>5</sub> and R<sub>6</sub> at each occurrence are independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; or  
wherein R<sub>5</sub> and R<sub>6</sub> and the nitrogen to which they are attached, at each occurrence form a 5 or 6 membered heterocycloalkyl ring; and  
wherein R<sub>7</sub> and R<sub>8</sub> are independently selected from the group consisting of H; -C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -OH, -NH<sub>2</sub>, and halogen; -C<sub>3</sub>-C<sub>6</sub>

cycloalkyl; -(C<sub>1</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl); -C<sub>2</sub>-C<sub>4</sub> alkenyl; and -C<sub>2</sub>-C<sub>4</sub> alkynyl;  
wherein each heteroaryl at each occurrence is optionally substituted with 1 or 2 R<sub>50</sub> groups;  
wherein each heterocycloalkyl group at each occurrence is optionally substituted with 1 or 2 groups that are independently R<sub>50</sub> or =O..

Claim 5. (original) A compound according to claim 1, wherein R<sub>2</sub> and R<sub>3</sub> are hydrogen.

Claim 6. (original) A compound according to claim 1, wherein R<sub>15</sub> is hydrogen.

Claim 7. (cancelled)

Claim 8. (Cancelled)

Claim 9. (original) A compound according to claim 8 wherein one of x<sub>1</sub>, x<sub>2</sub>, or x<sub>3</sub> is SO<sub>2</sub>.

Claim 10. (original) A compound according to claim 8 wherein one of x<sub>1</sub>, x<sub>2</sub>, or x<sub>3</sub> is NH.

Claim 11. (original) A compound according to claim 8 wherein x<sub>1</sub>, x<sub>2</sub>, and x<sub>3</sub> are each CH<sub>2</sub>.

Claim 12. (currently amended) A compound according to claim 1 selected from the group consisting of:

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyridine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyrazine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide;

3-amino-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-1,2,4-triazole-5-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-5-methylisoxazole-3-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-6-hydroxypyridine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-imidazole-4-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)nicotinamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-pyrazole-4-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)isonicotinamide;

5-chloro-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)thiophene-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-neopentyl-3,4-dihydro-2*H*-chromen-4-yl]amino}propyl)benzamide;

*N*-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-3,4-dihydro-2*H*-chromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-neopentyl-1,2,3,4-tetrahydroquinolin-4-yl]amino}propyl)benzamide;

*N*-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-1,2,3,4-tetrahydroquinolin-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1*S*)-7-neopentyl-1,2,3,4-tetrahydronaphthalen-1-

yl]amino}propyl)benzamide;

N- [(1S, 2R)-3- { [(1S)-7-tert-butoxy-1, 2, 3, 4-  
tetrahydronaphthalen-1-yl]amino}-1-(3, 5-difluorobenzyl)-2-  
hydroxypropyl]benzamide;

N-((1S, 2R)-1-(3, 5-difluorobenzyl)-2-hydroxy-3- { [(4R)-6-  
neopentyl-2, 2-dioxide-3, 4-dihydro-1H-isothiochromen-4-  
yl]amino}propyl)benzamide;

N- [(1S, 2R)-3- { [(4R)-6-tert-butoxy-2, 2-dioxide-3, 4-dihydro-  
1H-isothiochromen-4-yl]amino}-1-(3, 5-difluorobenzyl)-2-  
hydroxypropyl]benzamide;

N-((1S, 2R)-1-(3, 5-difluorobenzyl)-2-hydroxy-3- { [1-(3-  
neopentylphenyl)cyclohexyl]amino}propyl)benzamide;

N- [(1S, 2R)-3- { [1-(3-tert-butoxyphenyl)cyclohexyl]amino}-1-  
(3, 5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S, 2R)-1-(3, 5-difluorobenzyl)-2-hydroxy-3- { [1-(3-  
neopentylphenyl)cyclopropyl]amino}propyl)benzamide;

N- [(1S, 2R)-3- { [1-(3-tert-butoxyphenyl)cyclopropyl]amino}-1-  
(3, 5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S, 2R)-1-(3, 5-difluorobenzyl)-2-hydroxy-3- { [(4-  
neopentyl-1, 1'-biphenyl-2-yl)methyl]amino}propyl)benzamide;

N- [(1S, 2R)-3- { [(4-tert-butoxy-1, 1'-biphenyl-2-  
yl)methyl]amino}-1-(3, 5-difluorobenzyl)-2-  
hydroxypropyl]benzamide;

N- [(1S, 2R)-1-(3, 5-difluorobenzyl)-2-hydroxy-3- { (2-  
neopentyl-9H-fluoren-9-yl)amino}propyl]benzamide;

~~N-[(1S,2R)-3-[(2-tert-butoxy-9H-fluoren-9-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~  
~~N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-3,5-dimethylbenzamide; and~~  
~~N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide.~~

Claim 13. (canceled).

Claim 14. (previously presented) A method for the treatment or prevention of Alzheimer's disease comprising administration of a therapeutically effective amount of a compound or salt according to Claim 1, to a patient in need thereof.

Claim 15. (original) A method of treatment as in claim 14, wherein the patient is a human.

Claim 16. (cancelled)

Claim 17. (original) A pharmaceutical composition comprising a compound according to claim 1 in combination with a physiologically acceptable carrier or excipient.